Science For A Better Life

Clinical Study Synopsis

This Clinical Study Synopsis is provided for patients and healthcare professionals to increase the transparency of Bayer's clinical research. This document is not intended to replace the advice of a healthcare professional and should not be considered as a recommendation. Patients should always seek medical advice before making any decisions on their treatment. Healthcare Professionals should always refer to the specific labelling information approved for the patient's country or region. Data in this document or on the related website should not be considered as prescribing advice.
The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

Bayer

Clinical Trial Results Synopsis

Study Design Description		
Study Sponsor:	Bayer	
Study Number:	11586	NCT00667979
Study Phase:	IV Interventional	
Official Study Title:	A pilot, randomized, double-blind, placebo-controlled, crossover study evaluating the efficacy and safety of vardenafil versus placebo administered 12, 18, and 24 hours prior to initiation of sexual intercourse in subjects with ED	
Therapeutic Area:	Men' s Health	
Test Product		
Name of Test Product:	Vardenafil (Levitra, BAY38-9456)	
Name of Active Ingredient:	Vardenafil	
Dose and Mode of Administration:	10 mg or 20 mg tablet administered orally at the designated time intervals (12, 18, 24 hours).	
Reference Therapy/Placebo		
Reference Therapy:	Placebo	
Dose and Mode of Administration:	Matching placebo 10 mgadministered orally at the designated time intervals (24, 18, 12 hours).	
Duration of Treatment:	Subjects were requested to make two sexual intercourse attempts for each treatment per designated time interval; for a total of 12 attempts.	
Studied period:	**Date of first subjects' first visit:**	24 SEP 2004
	Date of last subjects' last visit:	07 DEC 2004
Premature Study Suspension / Termination:	No	
Substantial Study Protocol Amendments:	None	
Study Centre(s):	The study was conducted at 21 investigational sites (8 in Australia, 7 in Germany, and 6 in Italy).	
Methodology:	This is a randomized, double-blind, placebo-controlled, crossover study. Following screening, eligible subjects were challenged with vardenafil to determine their optimal dose (10 mg or 20 mg). The optimal dose of vardenafil was the one which produced an affirmative diary Sexual Encounter Profile Question 3 (SEP-3) response ("Did your erection last long enough for you to have successful intercourse?") for any sexual intercourse attempt made 0.5 to 6 hours after administration during the challenge phase as determined by the investigator and subject. This optimal dose of vardenafil was used during the randomized treatment phase of the study. Subjects were then randomized to treatment sequences detailing the order of study medication to be taken at the designated time intervals (12, 18, 24 hours) prior to sexual intercourse during the randomized treatment	

	phase of the study. Subjects attended the clinic six times over a period of approximately 8 weeks. Study visits occurred at Weeks -2, -1 and Weeks 0, 2, 4, and 6.
Indication/ Main Inclusion Criteria:	Indication: Erectile Dysfunction (ED) Main inclusion criteria: Males aged 18 - 64 years in a heterosexual relationship with a diagnosis of ED for more than 6 months. Eligible subjects had to make at least two attempts at sexual intercourse on two separate days during the untreated, run-in phase, have International Index of Erectile Function (IIEF)-5 score <22 at screening, and an affirmative SEP-3 response following a challenge dose of 10 mg or 20 mg vardenafil.
Study Objectives:	**Primary:** To evaluate the proportion of subjects receiving vardenafil 20 mg with successful completion of sexual activity following dosing with study medication at 12, 18, and 24 hours. **Secondary:** To evaluate the safety and tolerability of vardenafil when administered 12, 18, and 24 hours prior to attempts at sexual intercourse.
Evaluation Criteria:	**Efficacy (Primary):** Efficacy was measured by diary responses regarding maintaining an erection to successful completion of sexual intercourse (SEP-3) at each of the three time intervals following dosing with placebo or vardenafil. The primary efficacy endpoint was comparison of the proportion of subjects with at least one successful SEP-3 out of two possible sexual intercourse attempts at 12 (±2) hours for vardenafil and placebo treatments for the subset of subjects taking 20 mg. **Efficacy (Secondary):** • Proportion of subjects with at least one successful SEP-3 out of two possible sexual intercourse attempts at 18 (±2) hours and 24 (±2) hours, respectively, was compared for vardenafil and placebo treatments for the subset of subjects taking 20 mg. • Proportion of subjects with at least one successful SEP-3 out of two possible sexual intercourse attempts at 12, 18, and 24 hours (±2 hours each), respectively, was compared for vardenafil and placebo treatments for all evaluable subjects in the intent-to-treat (ITT) population. • Proportion of subjects with a successful SEP-3 on the first attempt at 12, 18, and 24 hours (±2 hours each), respectively, was compared for vardenafil and placebo. **Safety:** Safety assessments included adverse events (AEs), vital signs (heart rate and blood pressure), and physical examinations. Clinical laboratory tests (hematology and clinical chemistry) and electrocardiograms (ECGs) were performed at baseline.

Statistical Methods:	**Efficacy (Primary):** A Mainland-Gart test was used to compare the proportion of subjects with at least one successful SEP-3 in the designated time intervals (12, 18, or 24 hours post-dose) between the vardenafil and placebo treatments. A step-down approach was used to control the overall type I error rate associated with testing multiple hypotheses. The three hypotheses were tested in the following order: SEP-3 at 12 hours first, then 18 hours, then finally at 24 hours. Statistical analyses included the subject specific odds ratio and the 95% confidence interval around this estimate at each of the three time-points. **Efficacy (Secondary):** The proportion of subjects with at least one successful SEP-3 was compared for each treatment using Mainland-Gart test: • Based on attempts made at 18 (±2) hours and 24 (±2) hours after dosing separately for those subjects on the 20 mg dose • Based on attempts made at 12 (±2) hours, 18 (±2) hours and 24 (±2) hours after dosing separately for all evaluable subjects in the ITT Population • Based on the first attempt made for each treatment within 12 (±2), 18 (±2), and 24 (±2) hours after dosing separately for all evaluable subjects in the ITT Population and for a subject of those on the 20 mg dose **Safety:** Statistical tests were not conducted for safety variables.
Number of Subjects:	A total of 315 male subjects with ED were screened, 293 entered the challenge phase, 264 were randomized to double-blind treatment (78 vardenafil 10 mg and 186 vardenafil 20 mg), and 245 completed the study (69 vardenafil 10 mg, 176 vardenafil 20 mg).

Study Results

Results Summary — Subject Disposition and Baseline

Male subjects enrolled in this study had ED of varying etiology with a mean duration of 4 years since initial diagnosis. The majority of subjects were Caucasian (97%) and the mean age and body mass index was 53.5 years (range: 28 to 65) and 27.5 Kg/m^2 (range: 19 to 55). Most subjects enrolled in this study had moderate (34%) or mild-moderate (31%) ED at baseline; the mean baseline IIEF-5 total score was 10.5 indicating moderate ED. More investigators and subjects chose vardenafil 20 mg as their optimal dose (186 subjects) than 10 mg (78 subjects). More subjects randomized to vardenafil 20 mg treatment had severe ED (30%) than those randomized to 10 mg (14%).

Results Summary — Efficacy

In this pilot study, vardenafil 20 mg failed to demonstrate a statistically or clinically meaningful difference from placebo in the proportion of subjects with a successful SEP-3 at 12 (±2) hours post-dose (odds ratio = 1.33 [95% CI: 0.62 - 2.89]).

The majority of subjects in the 20 mg subset either responded to both treatments (40%) or failed both treatments (35%) at the 12 (±2) hour time-point.

Due to a statistically significant ($p<0.001$) carryover effect (i.e., treatment-by-period

interaction), Period 1 data (first treatment administered from Container A within a visit interval) were examined independent of Period 2 data (second treatment administered from Container B within a visit interval). Assessment of Period 1 data showed a statistically significant ($p<0.001$) and clinically meaningful (≥16%) difference between treatments at the 12 (±2) hour time-point, in favor of vardenafil 20 mg (odds ratio = 3.50 [95% CI: 1.74 - 7.04]).

Period 2 data were un-interpretable due to the effect that the first period appeared to have on the results of the second period.

Primary efficacy results for all subjects in the ITT Population (i.e., those who received vardenafil 10 mg or 20 mg) were comparable to those observed for the vardenafil 20 mg subset (odds ratio = 1.73 [95% CI: 0.92 - 3.29] at 12 [±2] hours). Assessment of Period 1 data for all subjects showed a statistically significant ($p\leq0.008$) and clinically meaningful (≥16%) difference between treatments at the 12, 18, and 24 (±2 each) hour time-points, in favor of vardenafil (odds ratios = 3.24, 2.40, and 2.08 respectively).

Results Summary — Safety

Vardenafil was well tolerated. Less than 20% of subjects reported a treatment-emergent AE after receiving any of the study treatments (14% vardenafil 10 mg challenge, 13% vardenafil 20 mg challenge, 17% placebo treatment, 14% vardenafil 10 mg treatment, and 19% vardenafil 20 mg treatment) and the majority of AEs were of mild or moderate intensity.

The most common (≥2%) treatment-emergent AEs experienced following vardenafil treatment were headache (4 - 6%), flushing (2 - 6%), dyspepsia (2 - 3%), and nasal congestion (0 - 2%). All four events are consistent with the safety profile and are described in the product labeling for vardenafil.

There was no apparent dose-related incidence of treatment-emergent AEs, drug-related AEs, or AEs of special interest between the 10 mg and 20 mg vardenafil doses.

There were no deaths during the conduct of the study. Treatment-emergent serious adverse events (SAEs) were reported for three subjects (arrhythmia and angina pectoris after the 20 mg challenge and epistaxis during placebo treatment).

Six subjects treated with vardenafil were discontinued from the study due to treatment-emergent AEs (two after the vardenafil 10 mg challenge, three after the vardenafil 20 mg challenge, and one during 20 mg treatment). Two subjects were withdrawn due to cardiac SAEs and the remaining four were withdrawn due to AEs consistent with the safety profile of vardenafil (e.g., headache, flushing, dyspepsia, nasal congestion).

Vardenafil had no clinically relevant effects on vital signs.

Conclusion(s)			
In this pilot study of 293 subjects, vardenafil 20 mg failed to demonstrate a statistically significant or clinically meaningful difference from placebo in the proportion of subjects with a successful SEP-3 at 12, 18, or 24 (±2 hours each) post-dose. This failure was perhaps due in part to the triple, two-way crossover study design, since a statistically significant carryover (i.e., treatment-by-period) effect was evident at the 12 hour time-point for all efficacy analyses. Due to the significant treatment-by-period interaction, an analysis of just Period 1 data (first treatment administered from Container A within a visit interval) at the 12 (±2) hour time-point was performed and disclosed a statistically significant ($p<0.001$) and clinically meaningful (≥16%) difference in favor of vardenafil 20 mg for the proportion of subjects with at least one successful SEP-3, but not at the 18 hour time-point. Vardenafil was well tolerated with the occurrence of common AEs consistent with that described in the product labeling for vardenafil.			
Publication(s):	None		
Date Created or Date Last Updated:	17 APR 2012	**Date of Clinical Study Report:**	02 JUN 2005

Product Identification Information

Product Type	Drug
US Brand/Trade Name(s)	Levitra, Staxyn
Brand/Trade Name(s) ex-US	Levitra, Vivanza, Yaila, Levitra 10mg orodispersible tablets, Staxyn, Vivanza 10mg orodispersible tablets, Vardenafil MK
Generic Name	Vardenafil hydrochloride
Main Product Company Code	BAY38-9456
Other Company Code(s)	
Chemical Description	2-[2-Ethoxy-5-(4-ethyl-piperazine-1-sulfonyl)-phenyl]-5-methyl-7-propyl-3H-imidazo[5,1-f] [1,2,4]triazin-4-one monohydrochloride trihydrate
Other Product Aliases	

Date of last Update/Change: 14 March 2016